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Interventions and Management

1. Comparison of a robotic-assisted gait training program with a program of functional gait training for children with cerebral palsy: design and methods of a two group randomized controlled cross-over trial.

Hilderley AJ, Fehlings D, Lee GW, Wright FV.

Springerplus. 2016 Oct 28;5(1):1886. eCollection 2016.

BACKGROUND: Enhancement of functional ambulation is a key goal of rehabilitation for children with cerebral palsy (CP) who experience gross motor impairment. Physiotherapy (PT) approaches often involve overground and treadmill-based gait training to promote motor learning, typically as free walking or with body-weight support. Robotic-assisted gait training (RAGT), using a device such as the Lokomat®Pro, may permit longer training duration, faster and more variable gait speeds, and support walking pattern guidance more than overground/treadmill training to further capitalize on motor learning principles. Single group pre-/post-test studies have demonstrated an association between RAGT and moderate to large improvements in gross motor skills, gait velocity and endurance. A single published randomized controlled trial (RCT) comparing RAGT to a PT-only intervention showed no difference in gait kinematics. However, gross motor function and walking endurance were not evaluated and conclusions were limited by a large PT group drop-out rate. **METHODS/DESIGN:** In this two-group cross-over RCT, children are randomly allocated to the RAGT or PT arm (each with twice weekly sessions for eight weeks), with cross-over to the other intervention arm following a six-week break. Both interventions are grounded in motor learning principles with incorporation of individualized mobility-based goals. Sessions are fully operationalized through manualized, menu-based protocols and post-session documentation to enhance internal and external validity. Assessments occur pre/post each intervention arm (four time points total) by an independent assessor. The co-primary outcomes are gross motor functional ability (Gross Motor Function Measure (GMFM-66) and 6-minute walk test), with secondary outcome measures assessing: (a) individualized goals; (b) gait variables and daily walking amounts; and (c) functional abilities, participation and quality of life. Investigators and statisticians are blinded to study group allocation in the analyses, and assessors are blinded to treatment group. The primary analysis will be the pre- to post-test differences (change scores) of the GMFM-66 and 6MWT between RAGT and PT groups. **DISCUSSION:** This study is the first RCT comparing RAGT to an active gait-related PT intervention in paediatric CP that addresses gait-related gross motor, participation and individualized outcomes, and as such, is expected to provide comprehensive information as to the potential role of RAGT in clinical practice. Trial registration ClinicalTrials.gov NCT02196298.

[PMID: 27843743](#)

2. Effect of Preoperative Indications Conference on Procedural Planning for Treatment of Scoliosis.

Chan CM, Swindell HW, Matsumoto H, Park HY, Hyman JE, Vitale MG, Roye DP Jr, Roye BD.

Spine Deform. 2016 Jan;4(1):27-32. doi: 10.1016/j.jspd.2015.05.003. Epub 2015 Dec 23.

STUDY DESIGN: This study determines the rate of change in the scoliosis surgery plan in cases presented in preoperative indications conference. **OBJECTIVES:** To determine the effect of preoperative indications conference on the plan of surgery and to identify characteristics that increased the likelihood of change. **SUMMARY OF BACKGROUND DATA:** Preoperative indications conferences are used as a teaching and planning tool. Levels of fusion, construct options, and necessity for osteotomies are often debated in the planning of scoliosis surgery. **METHODS:** Scoliosis surgeries were presented at preoperative indications conference with four attending pediatric orthopedic surgeons present. The operative surgeon committed to a surgical plan before conference. A consensus-based plan was made without knowledge of the operative surgeon's preconference plan. Changes of plan were classified as major, minor, or no change. **RESULTS:** Of the 107 surgical plans, 50 were index surgeries, 13 were revisions, and 44 were scheduled growing rod lengthenings. There were two major changes, including a change to a growing construct from planned fusion, and a change in fusion levels in an adolescent idiopathic scoliosis (AIS) patient. There were 13 minor changes, which included changes in fusion levels (1 to 3; mean = 1.23) and the addition of an osteotomy. The rate of change was 28% for index surgeries and 7.69% for revisions. Of the 14 changes in the 50 index surgeries, there were 8 AIS, 3 cerebral palsy, 1 congenital scoliosis, 1 Ehlers-Danlos, and 1 patient with an undetermined neuromuscular condition. There was 1 change in 13 revision surgeries. There were no changes for growing rod lengthenings and no cancellations as a result of indications conference. **CONCLUSIONS:** Although revision scoliosis surgery is complex, index AIS/JIS surgery was most subject to the influence of indications conference. This likely reflects controversy around choosing levels of fusion.

[PMID: 27852496](#)

3. Locomotor training through a novel robotic platform for gait rehabilitation in pediatric population: short report.

Bayón C, Lerma S, Ramírez O, Serrano JI, Del Castillo MD, Raya R, Belda-Lois JM, Martínez I, Rocon E.

J Neuroeng Rehabil. 2016 Nov 14;13(1):98.

BACKGROUND: Cerebral Palsy (CP) is a disorder of posture and movement due to a defect in the immature brain. The use of robotic devices as alternative treatment to improve the gait function in patients with CP has increased. Nevertheless, current gait trainers are focused on controlling complete joint trajectories, avoiding postural control and the adaptation of the therapy to a specific patient. This paper presents the applicability of a new robotic platform called CPWalker in children with spastic diplegia. **FINDINGS:** CPWalker consists of a smart walker with body weight and autonomous locomotion support and an exoskeleton for joint motion support. Likewise, CPWalker enables strategies to improve postural control during walking. The integrated robotic platform provides means for testing novel gait rehabilitation therapies in subjects with CP and similar motor disorders. Patient-tailored therapies were programmed in the device for its evaluation in three children with spastic diplegia for 5 weeks. After ten sessions of personalized training with CPWalker, the children improved the mean velocity (51.94 ± 41.97 %), cadence (29.19 ± 33.36 %) and step length (26.49 ± 19.58 %) in each leg. Post-3D gait assessments provided kinematic outcomes closer to normal values than Pre-3D assessments. **CONCLUSIONS:** The results show the potential of the novel robotic platform to serve as a rehabilitation tool. The autonomous locomotion and impedance control enhanced the children's participation during therapies. Moreover, participants' postural control was substantially improved, which indicates the usefulness of the approach based on promoting the patient's trunk control while the locomotion therapy is executed. Although results are promising, further studies with bigger sample size are required.

[PMID: 27842562](#)

4. Are electromyographic patterns during gait related to abnormality level of the gait in patients with spastic cerebral palsy?

Syczewska M, Świącicka A.

Acta Bioeng Biomech. 2016;18(3):91-96.

PURPOSE: One of the aims of the treatment in ambulant cerebral palsy (CP) patients is improvement of gait. The level of gait pathology is assessed by instrumented gait analysis, including surface electromyography. The aim of this study was to investigate the relation of the abnormality level of the gait and the co-contraction of the agonist-antagonist muscles, and relation between symmetry left /right leg in gait and symmetry of muscular activity. **METHODS:** Fifty one patients with cerebral palsy underwent clinical assessment and instrumented gait analysis, including surface electromyography. Signals were bilaterally collected from rectus femoris, medial and lateral hamstrings, tibialis anterior, lateral gastrocnemius and gluteus maximus. In older children additionally signals from soleus and lateral vastus were recorded. Sixteen gait variables were selected to calculate Gillette Gait Index, separately for left and right leg. From the envelopes a series of cross-correlation coefficients were calculated. **RESULTS:** Weak correlations were found between averaged agonist-antagonist correlation coefficient and Gillette Gait Index. Differences between hemiparetic less-involved legs, hemiparetic spastic legs, and diplegic legs were found for co-contraction of rectus femoris and biceps femoris and for averaged agonist-antagonist co-contraction. The differences between hemiparetic and diplegic groups were found for some muscle correlation coefficients. **CONCLUSIONS:** The results obtained in this study show that the activity pattern of the leg muscles is specific to a given patient, and the dependence of the kinematics pathology on the abnormal activation pattern is not a direct one.

[PMID: 27840431](#)

5. Wii-based interactive video games as a supplement to conventional therapy for rehabilitation of children with cerebral palsy: A pilot, randomized controlled trial.

Sajan JE, John JA, Grace P, Sabu SS, Tharion G.

Dev Neurorehabil. 2016 Nov 15:1-7. [Epub ahead of print]

OBJECTIVE: To assess the effect of interactive video gaming (IVG) with Nintendo Wii (Wii) supplemented to conventional therapy in rehabilitation of children with cerebral palsy (CP). **DESIGN:** Randomized, controlled, assessor-blinded study. **PARTICIPANTS:** Children with CP; 10 children each in the control and intervention groups. **INTERVENTION:** IVG using Wii, given as a supplement to conventional therapy, for 45 min per day, 6 days a week for 3 weeks. The children in the control group received conventional therapy alone. **OUTCOME MEASURES:** Posture control and balance, upper limb function, visual-perceptual skills, and functional mobility. **RESULTS:** Significant improvement in upper limb functions was seen in the intervention group but not in the control group. Improvements in balance, visual perception, and functional mobility were not significantly different between control and intervention groups. **CONCLUSIONS:** Wii-based IVG may be offered as an effective supplement to conventional therapy in the rehabilitation of children with CP.

[PMID: 27846366](#)

6. A Battery of Motor Tests in a Neonatal Mouse Model of Cerebral Palsy.

Feather-Schussler DN, Ferguson TS.

J Vis Exp. 2016 Nov 3;(117). doi: 10.3791/53569.

As the sheer number of transgenic mice strains grow and rodent models of pediatric disease increase, there is an expanding need for a comprehensive, standardized battery of neonatal mouse motor tests. These tests can validate injury or disease models, determine treatment efficacy and/or assess motor behaviors in new transgenic strains. This paper presents a series of neonatal motor tests to evaluate general motor function, including ambulation, hindlimb foot angle, surface righting, negative geotaxis, front- and hindlimb suspension, grasping reflex, four limb grip strength and cliff aversion. Mice between the ages of post-natal day 2 to 14 can be used. In addition, these tests can be used for a wide range of neurological and neuromuscular pathologies, including cerebral palsy, hypoxic-ischemic encephalopathy, traumatic brain injury, spinal cord injury, neurodegenerative diseases, and neuromuscular disorders. These tests can also be used to determine the effects of pharmacological agents, as well as other types of therapeutic interventions. In this paper, motor deficits were evaluated in a

novel neonatal mouse model of cerebral palsy that combines hypoxia, ischemia and inflammation. Forty-eight hours after injury, five tests out of the nine showed significant motor deficits: ambulation, hindlimb angle, hindlimb suspension, four limb grip strength, and grasping reflex. These tests revealed weakness in the hindlimbs, as well as fine motor skills such as grasping, which are similar to the motor deficits seen in human cerebral palsy patients.

[PMID: 27842358](#)

7. Prognostic predictors for ambulation in children with cerebral palsy: a systematic review and meta-analysis of observational studies.

Keeratisiroj O, Thawinchai N, Siritaratiwat W, Buntragulpoontawee M, Pratoomsoot C.

Disabil Rehabil. 2016 Nov 16:1-9. [Epub ahead of print]

PURPOSE: The purpose of this study is to investigate the prognostic predictors for ambulation in children with cerebral palsy using meta-analysis of observational studies. **METHOD:** Electronic searches were conducted in PubMed, SCOPUS, CINAHL, ProQuest, Ovid, Wiley InterScience, and ScienceDirect databases from their start dates to December 2015. **RESULTS:** Of the 1123 identified articles, 12 met the inclusion criteria for qualitative synthesis, eight of which were deemed appropriate for meta-analysis. Qualitative synthesis found that the type of cerebral palsy, early motor milestones, primitive reflexes and postural reactions, absence of visual impairment, absence of intellectual disability, absence of epilepsy or seizure, and ability to feed self were indicated as potential predictors for ambulation. Meta-analysis detected four significant prognostic predictors for ambulation: sitting independently at 2 years, absence of visual impairment, absence of intellectual disability, and absence of epilepsy or seizure. **CONCLUSION:** These prognostic predictors should be taken into consideration in therapeutic plans and rehabilitation goals, especially sitting independently before the age of 2 years. Implications for rehabilitation The meta-analysis supports strong evidence that sitting independently at 2 years of age, absence of visual impairment, absence of intellectual disability, and absence of epilepsy or seizure are positive predictors for ambulation in children with cerebral palsy. The therapeutic plans and rehabilitation goals should be considered cautiously for these predictors, especially sitting independently before the age of two years.

[PMID: 27848255](#)

8. Gastroesophageal Reflux in Neurologically Impaired Children: What Are the Risk Factors?

Kim S, Koh H, Lee JS.

Gut Liver. 2016 Nov 14. doi: 10.5009/gnl16150. [Epub ahead of print]

BACKGROUND/AIMS: Neurologically impaired patients frequently suffer from gastrointestinal tract problems, such as gastroesophageal reflux disease (GERD). In this study, we aimed to define the risk factors for GERD in neurologically impaired children. **METHODS:** From May 2006 to March 2014, 101 neurologically impaired children who received 24-hour esophageal pH monitoring at Severance Children's Hospital were enrolled in the study. The esophageal pH finding and the clinical characteristics of the patients were analyzed. **RESULTS:** The reflux index was higher in patients with abnormal electroencephalography (EEG) results than in those with normal EEG results ($p=0.027$). Mitochondrial disease was associated with a higher reflux index than were epileptic disorders or cerebral palsy ($p=0.009$). Patient gender, feeding method, scoliosis, tracheostomy, and baclofen use did not lead to statistical differences in reflux index. Age of onset of neurological impairment was inversely correlated with DeMeester score and reflux index. Age at the time of examination, the duration of the disease, and the number of antiepileptic drugs were not correlated with GER severity. **CONCLUSIONS:** Early-onset neurological impairment, abnormal EEG results, and mitochondrial disease are risk factors for severe GERD.

[PMID: 27840365](#)

9. [Cytoflavin in the treatment of preschool and early school age children with the consequences of perinatal hypoxic brain damages].

[Article in Russian]

Lavrik SY, Shprakh VV, Domitruk SV, Borisov AS.

Zh Nevrol Psikhiatr Im S S Korsakova. 2016;116(10):34-37.

AIM: To study the efficacy and safety of the complex metabolic neuroprotector cytoflavin in children with the consequences of perinatal hypoxic brain damages. MATERIAL AND METHODS: Patients, aged 4-8 years, were stratified into three groups: 35 with infant cerebral palsy, 64 with the minimal brain dysfunction and 47 with sensorineural hearing loss. The control group consisted of 30 children. Monotherapy with cytoflavin was carried out in the dose of one tablet twice a day for 25 days. Neurologic status, neurophysiological examination and neuropsychophysiological testing were performed before and after treatment. RESULTS AND CONCLUSION: The efficacy of cytoflavin in children of preschool and early school age was demonstrated. A complex neuroprotective action, including vasoactive, nootropic and antiasthenic effects, was revealed. Side-effects of cytoflavin were not observed.

[PMID: 27845313](#)

Prevention and Cure

10. A magnetic resonance imaging finding in children with cerebral palsy: Symmetrical central tegmental tract hyperintensity.

Derinkuyu BE, Ozmen E, Akmaz-Unlu H, Altinbas NK, Gurkas E, Boyunaga O.

Brain Dev. 2016 Nov 11. pii: S0387-7604(16)30173-5. doi: 10.1016/j.braindev.2016.10.004. [Epub ahead of print]

BACKGROUND: Central tegmental tract is an extrapyramidal tract between red nucleus and inferior olivary nucleus which is located in the tegmentum pontis bilaterally and symmetrically. The etiology of the presence of central tegmental tract hyperintensity on MRI is unclear. PURPOSE: In this study our aim is to evaluate the frequency of central tegmental tract lesions in patients with cerebral palsy and control group, as well as to determine whether there is an association between central tegmental tract lesions and cerebral palsy types. MATERIALS AND METHODS: Clinical and MRI data of 200 patients with cerebral palsy in study group (87 female, 113 male; mean age, 5.81years; range, 0-16years) and 258 patients in control group (114 female, 144 male; mean age, 6.28years; range, 0-16years) were independently evaluated by two reader for presence of central tegmental tract hyperintensity and other associated abnormalities. RESULTS: Central tegmental tract hyperintensities on T2WI were detected in 19% of the study group (38/200) and 3.5% of the control group (9/258) ($p < 0.0001$). Among the total of 38 central tegmental tract lesions in study group, the frequency of central tegmental tract hyperintensity was 16% (24/150) in spastic cerebral palsy and 35% (14/40) in dyskinetic cerebral palsy ($p = 0.0131$). CONCLUSION: The prevalence of central tegmental tract hyperintensity is higher in patients with cerebral palsy particularly in dyskinetic type. We suggest that there is an increased association of the tegmental lesions with dyskinetic CP. Patients with cerebral palsy and ischemic changes were more likely to have central tegmental tract lesions. According to our results we advocate that an ischemic process may have a role in the etiopathogenesis.

[PMID: 27843044](#)

11. Integrative analysis of genetic data sets reveals a shared innate immune component in autism spectrum disorder and its co-morbidities.

Nazeen S, Palmer NP, Berger B, Kohane IS.

Genome Biol. 2016 Nov 14;17(1):228.

BACKGROUND: Autism spectrum disorder (ASD) is a common neurodevelopmental disorder that tends to co-occur with other diseases, including asthma, inflammatory bowel disease, infections, cerebral palsy, dilated cardiomyopathy, muscular dystrophy, and schizophrenia. However, the molecular basis of this co-occurrence, and whether it is due to a shared component

that influences both pathophysiology and environmental triggering of illness, has not been elucidated. To address this, we deploy a three-tiered transcriptomic meta-analysis that functions at the gene, pathway, and disease levels across ASD and its co-morbidities. **RESULTS:** Our analysis reveals a novel shared innate immune component between ASD and all but three of its co-morbidities that were examined. In particular, we find that the Toll-like receptor signaling and the chemokine signaling pathways, which are key pathways in the innate immune response, have the highest shared statistical significance. Moreover, the disease genes that overlap these two innate immunity pathways can be used to classify the cases of ASD and its co-morbidities vs. controls with at least 70 % accuracy. **CONCLUSIONS:** This finding suggests that a neuropsychiatric condition and the majority of its non-brain-related co-morbidities share a dysregulated signal that serves as not only a common genetic basis for the diseases but also as a link to environmental triggers. It also raises the possibility that treatment and/or prophylaxis used for disorders of innate immunity may be successfully used for ASD patients with immune-related phenotypes.

[PMID: 27842596](#)

12. Association of Maternal Obesity with Child Cerebral Palsy or Death.

McPherson JA, Smid MC, Smiley S, Stamilio DM.

Am J Perinatol. 2016 Nov 17. [Epub ahead of print]

Objective The primary aim of this study was to determine if there is an association between maternal obesity and cerebral palsy or death in children. **Study Design** This is a retrospective cohort analysis of a randomized controlled clinical trial previously performed by the Maternal-Fetal Medicine Units Network. Women in the original trial were included if at high risk for preterm delivery. The present study included singletons enrolled in the original study with complete data. Obese and nonobese women were compared. A secondary analysis comparing class 3 obese or classes 1 to 2 obese women to nonobese women was performed. The primary outcome was a composite of cerebral palsy or perinatal death. **Results** In this study, 1,261 nonobese, 339 obese, and 69 morbidly obese women were included. When adjusted for gestational age at delivery and magnesium exposure, there was no association between maternal obesity and child cerebral palsy or death. In the analysis using obesity severity categories, excess risk for adverse outcome appeared confined to the class 3 obese group. **Conclusion** In women at high risk of delivering preterm, maternal obesity was not independently associated with child cerebral palsy or death. The association in unadjusted analysis appears to be mediated by preterm birth among obese patients.

[PMID: 27855463](#)